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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,156	02/13/2006	Marta Rodriguez-Franco	SONN:087US	5874

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EXAMINER	
PAGE, BRENT T	

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1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,156	RODRIGUEZ-FRANCO ET AL.	
	Examiner	Art Unit	
	Brent Page	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/28/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of SEQ ID NO: 13 in the reply filed on 07/20/2007 is acknowledged. The traversal is on the ground(s) that unity of invention is present and that no prior art was presented. This is not found persuasive because each nucleic acid sequence is deemed to be a separate structure which constitutes a separate invention as stated in the restriction requirement. Furthermore, the art used in the rejection below does, in fact constitute prior art of wild-type moss promoting regions. Discussion of search burden does not apply to PCT rules on unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 23-52 are examined on the merits in the office action below.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. There are two instances of embedded hyperlink in paragraph 112 and paragraph 188 of the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 26 is objected to because of the following informalities: The claim contains nonelected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 13 for function as a promoter from Physcomitrella patens, does not reasonably provide enablement for all expression promoting regions from all mosses as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to an isolated DNA molecule and a method for the expression of a recombinant polypeptide product, comprising said molecule, wherein said molecule is a promoter-effective DNA molecule that encodes a "nucleus-derived" moss expression promoting region from any moss.

In contrast, Applicants disclose SEQ ID NO: 13 from Physcomitrella patens operably linked to a reporter gene, rhVEGF121, wherein function has only been shown in nonregenerating Physchomitrella patens protoplasts and in stable transgenic lines of Physcomitrella patens. Not other moss species have been transformed with said promoter sequence, and no sequences from other moss species have been demonstrated to function as a promoter by Applicants.

The function of promoter fragments and sequence variants in transgenic plants is unpredictable. Kim et al (1994, Plant Molecular Biology 24:105-117) in a mutational analysis of the nopaline synthase promoter in a stable transformation system, found that mutation of a single nucleotide significantly altered the strength of expression, while deletions in other regions of the promoter completely eliminated function (page 108 first full paragraph).

Deletion analysis of promoters is unpredictable. Donald et al (1990, EMBO J. 9:1717-1726) teach that a crucial promoter element for the *Arabidopsis* rcbS-1A promoter is located in the region about 250 bases upstream of the transcription initiation site.

Furthermore, the function of promoter fragments and sequence variants in transgenic plants is unpredictable wherein the promoter function is regulated by conditional elements. Dolferus et al (1994, Plant Physiology 105:1075-1087) in a deletion analysis of the *Arabidopsis Adh* promoter, found that deletion of different elements of the promoter affected promoter function conditional to the stress that was applied to the given promoter fragment (page 1080, last full paragraph and page 1082 first full paragraph).

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate all promoter-effective molecules from all mosses as broadly claimed.

Claims 23-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to millions of isolated sequences from multiple species of moss and methods of using the multitudes of embodiments of said sequences.

In contrast, the specification only describes SEQ ID NOs 1-27 as moss expressing promoter regions. The specification does not provide the description of the structures responsible for the function of promoting regions that are unique to moss, nor does the specification differentiate what structures are responsible for functioning embodiments versus non-functioning embodiments.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed

genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP section 2163, page 174 of chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in

possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites "An isolated nucleic acid molecule encoding a wild-type, nucleus-derived moss expression promoting region (MEPR)". It is unclear how an expression promoting region is "encoded". The term "encoding" typically refers to the DNA or mRNA which "encodes" proteins. It is unclear whether Applicants are referring to something other than a promoter which is present in the genomic DNA and promotes transcription of the mRNA, or if Applicants meant to limit the claim to a promoter sequence.

Claims 24-52 either depend directly or indirectly from claim 23 and therefore contain the same limitation and are thus rejected under 35 USC 112 second paragraph, for being indefinite.

For the purposes of examination, the Examiner is interpreting the claims to be drawn to promoter sequences. If this is an incorrect interpretation, Applicants are required to clarify what is meant by claim 23 in regard to "encoding".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-28 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Henschel et al (2002 Mol. Biol. Evol. 19:801-814).

The claims are broadly drawn to any isolated nucleic acid that "encodes" a wild-type "nucleus-derived" moss expression promoting region comprising a selection marker and further comprising at least "one sequence" that is homologous to genomic sequences of a species to be transformed.

The breadth of the claim "one sequence" is interpreted by the Examiner to read on as little as 2bp of sequence, and is therefore likely to read on any sequence of the isolated nucleic acid in question, and would therefore meet the limitation of the claim. Furthermore the phrase "a" sequence of SEQ ID NO: 13 reads on any 2 bp of SEQ ID NO: 13 rather than the full-length sequence.

Henschel et al teach the isolation of genes from Physcomitrella patens, including their promoter regions which are cloned into bluescript (a selection marker for bacteria transformation) see page 804 the first two full paragraphs in particular which describes the isolation and cloning of promoter fragments from Physcomitrella patens. Physcomitrella patens is classified as a moss and therefore the promoter fragments

meet the limitation of including a moss promoter and since the promoter is not translated, this region also inherently meets the limitation of comprising a 5' UTR. Since the limitation states "and/or" for the other elements, this meets the limitation of claim 28. Additionally, the cited promoter sequences would inherently comprise "a" sequence of SEQ ID NO: 13 wherein "a" sequence is as little as 2bp of SEQ ID NO:13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-28 and 33-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over henschel et al ((2002 Mol. Biol. Evol. 19:801-814) in view of Komano et al (US Patent 4710461).

The claims are broadly drawn to any isolated nucleic acid that "encodes" a wild-type "nucleus-derived" moss expression promoting region comprising a selection marker and further comprising at least "one sequence" that is homologous to genomic sequences of a species to be transformed.

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Henschel et al do not teach the above isolated promoter operably linked to recombinant polypeptide products and methods of isolating the expressed recombinant polypeptide product.

Komano et al teach a promoter isolated from *Marchantia polymorpha* which is operably linked to the recombinant polypeptides from *E. coli* and expressed in *E. coli*, and more specifically teach the moss promoter in a vector designed for the expression of recombinant DNA (see claims and Column 4 lines 1-69, for example). Komano et al further teach "...that is, the frequency of transcription in forming a RNA from a DNA, or the activity of the promoter, differs with the kind of promoter, and when DNA containing a promoter is used as a vector for molecular breeding, a promoter having a higher activity is advantageous. Furthermore, since a passenger, namely exogenous DNA, is

integrated in the vector, it is preferable that the size of the promoter be small...Therefore, development of a new promoter is always desired."

Given the state of the art and the disclosures by Henschel et al and Komano et al it would have been obvious to use the promoter disclosed by Henschel et al in plants as disclosed by Henschel et al to express recombinant polypeptides as disclosed and suggest by Komano et al for industrial production, for screening and defining consensus sequences etc as broadly claimed and as suggested by Komano et al. The expression of recombinant polypeptides is well known in the art and one or ordinary skill in the art would appreciate all of the applications of use for the promoters disclosed by Henschel et al and Komano et al and would have had a reasonable expectation of success.

Claims 29-32 are free of the prior art given the failure of the prior art to teach or reasonably suggest the isolated nucleic acid molecule wherein the molecule comprises promoting activity at least equal to CaMV 35 S promoter or 200%, 500% or 1000% of said promoter respectively.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brent Page whose telephone number is (571)-272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brent T Page

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER

Russell Kallis